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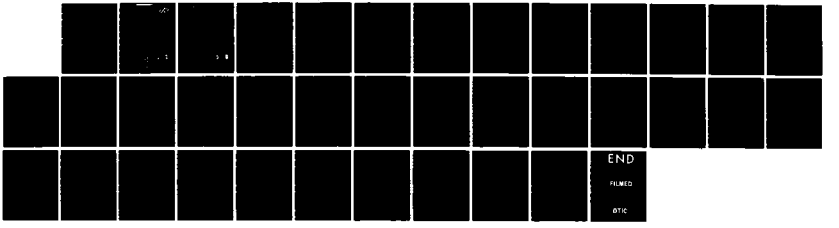

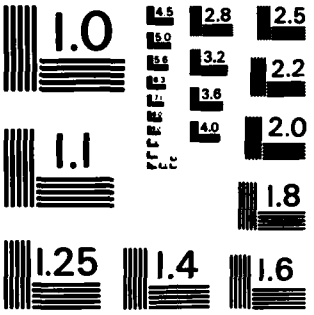

RESEARCH AND DEVELOPMENT OF WOUND DRESSING IN MAXILLOFACIAL TRAUMA

ANNUAL REPORT

BIOTEK, Inc.

21-C Olympia Avenue, Woburn, MA 01801 Tel: (617) 938-0938

AD_____

Report No. 2110-6

RESEARCH AND DEVELOPMENT OF WOUND DRESSING IN MAXILLOFACIAL TRAUMA

ANNUAL REPORT

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March 14, 1983

Supported by:
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BIOTEK, Inc.
21-C Olympia Avenue
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The base forms of lidocaine and bupivacaine were incorporated into powder and non-woven fabric forms of wound dressings. An antiseptic formulation of benzalkonium chloride (Maquat LC-12S) was also incorporated into fabrics and powders. The povidone iodine (BASF 17/12) was microencapsulated using the Wurster process. Selected materials were characterized by mercury porosimetry, electron diffraction of x-rays (EDAX), and stability to various storage conditions.

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The base forms of etidocaine and bupivacaine dissolved slowly in phosphate buffer. This rate could be decreased further by incorporation into powders and fabrics. Powders of bupivacaine base yellowed with age.

Benzalkonium chloride at a 20% concentration in fabric gave the best *in vitro* release (20% immediate release, 35% in one day and 45% in two days).

Continued active iodine release was demonstrated by microcapsules containing povidone iodine. At 30% polymer, 70% of the product was between 212-600 microns. This material gave *in vitro* release of approximately 17% in 1 hour, 47% in 1 day, 60% in 2 days, 70% in 3 days and 90% in 6 days. The diffusion was studied at 20°C to avoid the loss of active iodine during the study.

Samples of povidone iodine, benzalkonium chloride and control (poly-L(-) lactide) fabrics were sent to USAIDR for *in vivo* studies involving wound sepsis and healing. Microcapsules of povidone iodine will also be submitted.

FOREWARD

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

I. SUMMARY

The base forms of lidocaine and bupivacaine were incorporated into powder and non-woven fabric forms of wound dressings. An antiseptic formulation of benzalkonium chloride (Maquat LC-12S) was also incorporated into fabrics and powders. The povidone iodine (BASF 17/12) was microencapsulated using the Wurster process. Selected materials were characterized by mercury porosimetry, electron diffraction of x-rays (EDAX), and stability to various storage conditions.

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II. ACCOMPLISHMENTS

A. Material Preparation and Physical Characterization

1. Polylactide

During the present contract period we have continued to use the polymer blend (poly-L(-)lactide of R.S.V.=1.19 dl/g) which was described in the previous report (Report No. 2110-3, pp. 5-9). Additional polymer of 1.2±0.6 dl/g is available which can be used to obtain a blend of 1.2±0.1 dl/g. This will be blended when more polymer is required.

2. Benzalkonium Chloride

Potential suppliers of benzalkonium chloride preparations were contacted. Discussions with Sterling-Winthrop personnel indicated that the alkyl group should be approximately n-C_{14}. However, no unformulated benzalkonium chloride was available. Mason Chemical Company was suggested as a primary supplier of quaternary ammonium complexes. Mr. DeWolf was very helpful in describing various commercially available materials and the fabric (e.g., diaper) bacteriostatic formulations. Mason Chemical Company supplied three standard formulations which were 80% solids in an isopropanol-water solvent. The solids are:

Product	Percent of C_{12}	C_{14}	C_{16}	C_{18}
Maquat LC-12S	61	23	11	5
Maquat MC-1416	5	60	30	5
Maquat MC-1412	40	50	10	-

Mr. DeWolf indicated that LC-12S is the standard benzalkonium chloride of commercial interest.

Small quantities of benzalkonium chloride are required for bacteriostatic efficacy. Zephiran^{R} is sold as a 1/750 dilution (1,333 ppm). This concentration is required for Pseudomonas bacteriocidal activity. For diapers about 400 ppm is used, which corresponds to approximately 20 $\mu g/cm^2$.

The solvent was evaporated from the three Maquat samples and calibration curves were generated at the ultraviolet wavelength maximum of 262 nm.

3. Anesthetic Base Preparation

In the Annual Report, June 23, 1982, Report No. 2110-3, it was shown that the base forms of the amide anesthetics are released in a more continuous manner than are the drug hydrochlorides. The lidocaine and etidocaine drugs are available in both hydrochloride and base forms. Bupivacaine (base) was prepared from the hydrochloride by precipitation with NaOH in water. The end point was measured by monitoring the pH of the resulting suspension. The crystals were collected in a Buchner funnel, washed with water, and dried under vacuum.

4. Preparation of Powders

Films were prepared with polylactide and drug, cut into squares, and sent to the Massachusetts College of Pharmacy for grinding in a Mikro-Pulverizer with dry ice. A 20-mesh sieve was used as the classifier screen. Since Dr. Suva Roy has left the college Dr. Robert Mendes prepared the samples. The yields were remarkably high as shown in Table 1.

The film of bupivacaine (base) became yellow after a few days. Similarly the powder turned a deep yellow with age.

5. Preparation of Non-Woven Fabric

A series of experiments were performed to determine the spraying characteristics of solutions which yielded the type of non-woven fabric tested during this contract. Initial experiments were performed with polymer only. Later experiments included various concentrations of lidocaine-HCl at a constant polymer concentration in methylene chloride.

In the initial experiments, five grams of polymer were sprayed at the target from various concentrations in methylene chloride. The viscosities of these solutions were measured using a falling ball viscometer. This was correlated with the time required to spray the solution through the atomizing nozzle. The density of the solution was also measured, but it remained constant (1.29 gm/cm^3). A sample of fabric was cut with a punch and weighed and measured. The thickness was approximated using vernier calipers, since the standard Ames thickness gauge severely compressed the sample. A density was calculated from the thickness, area, and weight. The data are shown in Table 2.

TABLE 1

SIZE DISTRIBUTION OF PREPARED DRUG POWDERS

(Data is % of Total Milled Sample)

Size (μm)	20% Etidocaine (base)	20% Bupivacaine (base)
> 600	17.3	12.3
600-425	36.4	37.0
425-300	16.8	20.4
300-212	10.4	12.9
212-150	9.3	9.6
150-106	5.8	5.3
106-74	1.9	1.6
74-35	0.8	0.6
< 38	0.1	0.0
Percent Yield of Milling	92.9	91.9

TABLE 2

SPRAYING OF NON-WOVEN FABRIC OF POLYMER

Solution Concentration (g/100 ml)	Solution Viscosity (cps)	Spray Time (sec/5 gm)	Sample Weight ($mg/3\ cm^2$)	Sample Thickness (cm)	Sample Density (mg/cm^3)
9	16.1±0.2	112	40	0.28	60
10	22.5±0.0	121	31	0.16	81
11	29.1±0.4	129	56	0.47	50
12	42.0±0.2	150	61	0.41	62
13	(57)*	175	59	0.50	49

* calculated from spray time

A linear relationship was found between the solution viscosity and spraying time:

$$\eta = 16.2t - 16.6$$

where, η is viscosity in centipoise
and t is seconds/milliliter of solution.
The correlation coefficient was r = 0.9997.

Less fibrous product was collected in the center of the target when the solution concentration was lower. The density of the fabric may also be higher when the solution concentration is lower. The combination leads to much less visible fabric at lower concentrations.

At 11% polymer in methylene chloride, various drug/polymer ratios were sprayed. Lidocaine-HCl was sprayed at 5, 10, 20, 40% drug loadings as shown in Table 3. Again the more concentrated solutions gave the greater quantities of collected fabric. However, the solution density, viscosity, and spraying times were all similar. Since the mat thicknesses were about the same, the fabric densities were highest for the fabrics with the most drug (see Table 3).

6. Microencapsulation of Povidone-Iodine

Povidone iodine composites have not released active iodine in a continuous manner. Composite powders have had segregated areas of drug and polymer. Most of the drug has been released very rapidly from these powders, at 20% drug loading. Non-woven fabric material has held the drug more firmly. At 20% loading, almost no release is obtained, but at 40% a rapid partial release is observed.

To improve the active iodine release from the powders, these materials have been coated with a layer of polymer using the Wurster coating equipment, as used in Contract DAMD17-81-C-1195. This approach can theoretically yield zero-order drug release.

A composite of 80% drug and 20% polymer was prepared as an evaporated film from methylene chloride. This film was hard, but friable, and was coarsely ground with a mortar and pestle. This powder was then ground with a pestle on a 500 micron sieve. The resulting material was then ground through a 250 micron sieve. The final size distribution of this core powder is shown in Table 4.

This powder was coated with an additinal 10% of polymer, and a representative sample was obtained from the bed (see Table 5). Coating was continued to 20% polymer and another sample was taken. At this point the bed contained more material than it

TABLE 3

SPRAYING OF NON-WOVEN FABRIC WITH LIDOCAINE

(11% Polymer in Methylene Chloride)

Lidocaine-HCl % of Polymer	Sample Weight (mg/3 cm^2)	Sample Thickness (cm)	Sample Density (mg/cm^3)
5	43±10	0.36±0.05	64±4
10	70±18	0.46±0.09	62±5
20	96±25	0.44±0.12	103±23
40	118±22	0.42±0.10	131±20

TABLE 4

PVP-I_2 (BASF 17/12) MICROCAPSULE SIZE DISTRIBUTION

(Values are % of weight in each sieve fraction)

Microcapsule Size Range (μm)	20% Polymer Core	% Core in Microcapsules		
		90%	80%	71%*
> 600	0	0	1.2	4.4
425-600	0	0.2	12.0	17.7
300-425	0.9	2.7	31.7	35.0
212-300	37.2	64.0	26.5	17.4
150-212	18.6	14.4	11.4	6.8
106-150	15.6	7.3	8.4	6.5
75-106	11.8	5.7	4.8	6.5
38-75	10.1	5.6	3.9	5.6
< 38	5.9	0	0	0

* Does not include brush-down material

TABLE 5

PROCESSING SUMMARY OF PVP-I_2 (BASF 17/12) MICROENCAPSULATION

(Run 11-5)

Process Polymer %	Starting Weights: Starting Sample g	Starting Weights: Polymer Added g	Final Weight: MC g	Final Weight: (as drug) (g)	Losses: Wurster Holdup g	Losses: Oversize Removed g (500μm)	Losses: Sieve + Bag g	Losses: Samples Removed g
0-10	230***	26	80	(58)	176	-	-	26
10-20	54	27	190	(122)	-109	-	-	32
20-29	158	23	131	(74)	50	-	-	131
			(68)	(38)	-68*			68*
TOTALS		76			49			257**
	A	B	C		D	E	F	G

Material Balance: In: 184 g drug + 122 g polymer = 306 g
Out: 257 g samples + 49 g Wurster holdup = 306 g

Yield at 30% is 61% based on drug [not including samples purposefully removed, (74 + 38)/18.4] **
Yield at 30% is 84% based on samples/input materials [257/(230+76)]**

$$D_n = A_n + B_n - C_n \qquad A_{nil} = C_n - (E_n + F_n + G_n)$$

* Brush down of Wurster unit yields 68 grams
** Includes brushed-down material
*** Starting sample contains 20% polymer (46 g polymer and 184 g of drug)

did at the 10% loading. The coating operation was restarted and the final sample was obtained at 30% coating. A brush-down of the Wurster equipment yielded another 68 grams of product. The size distribution of the microcapsules is shown in Table 4.

7. Surface Concentration of Iodine in PVP-I_2-Polymer Powders

When writing the Annual Report, June 23, 1982, it was evident that an EDAX (energy dispersive analysis of X-rays) of PVP-I_2 powder was needed to complete the analysis. This analysis shows significant segregation of iodine within the sample (20% BASF 17/12, 212-300 microns), with about 50 counts/second at the iodine peak of a round particle that may be pure PVP-I_2. Background levels (2 counts/sec) were observed in the fibrous area of the sample.

On similar projects, mercury porosimetry has been found to yield useful information on microcapsule morphology. A single test gives information on (1) bulk density, by a repeatable method on a small sample, (2) interparticle void volume, (3) pore volume, with volume associated with various restricted pore radii, and (4) skeletal density which defines closed pore volumes assuming that the absolute density of the material is known. We sent samples of powders and fabrics to Micromeritics, Inc. who do porosimetry testing on a purchase order basis.

The bulk volume of the fabrics are dependent on the method of measurement, since the material is extremely compressible. Using vernier calipers and no compression the fabric volume was 3.32 cm^3/gm. After loading the porosimeter tube with mercury at atmospheric pressure the volume was 1.28 cm^3/gm. In general, volumes larger than 123 microns in diameter are filled by the porosimeter prior to the application of pressure.

The data on the equivalent volumes for particles and fabrics of 15% etidocaine-HCl are shown in Table 6. For a bed of particles of 300-425 microns sieve size we assume that volumes with equivalent pore sizes of more than 10 microns are interparticle voids. Constrictions of less than 10 microns are considered pore volumes. For non-woven fabric matrices the concept must change to the filtration effectiveness of a bed filter. SEM data indicate relatively smooth surfaces for all of the non-woven fabrics.

Physical property information is most useful as a quality control parameter or as a correlating parameter with <u>in vitro</u> drug release or a useful <u>in vivo</u> property.

TABLE 6

MERCURY POROSIMETRY VOLUMES OF
ETIDOCAINE HCl POWDERS AND FABRICS

	15% Etidocaine-HCl 300-425 μm Powder Particles cm^3/gm	15% Etidocaine-HCl Fabric cm^3/gm
Bulk Volume (calipers)	---	3.32
Bulk Volume (porosimeter)	1.218	1.285
Skeletal Volume	0.773	0.641
Intrusion Volume	0.313	0.644
Interparticle (>10 μm)	0.248	0.408
Pores (<10 μm)	0.065	0.236
1.0 - 10 μm	0.008	0.025
0.1 - 1.0 μm	0.008	0.074
<0.1 μm	0.049	0.137

B. In Vitro Drug Release

1. Calculation of Etidocaine and Bupivacaine Release

Etidocaine and bupivacaine have been analyzed in acidified buffer solutions and the analyzed sample has been discarded. As saturation of the buffer is approached, the entire buffer solution is changed. This generates a very complex calculation for the amount of drug released. In these calculations a least squares curve fit was used for a drug calibration. The small intercept that was generated sometimes caused the release to appear to continue when the actual absorbance values remained constant. It also unnecessarily increased the complexity of the calculation.

During this contract period we forced the calibration curve through the origin and obtained a best slope in absorbance units per μg of drug per ml of solution. A computer program was then written to accommodate drug diffusing into 40 ml of solution, removing 2.8 ml, acidifying with 0.2 ml of acid and discarding either the analyzed sample or the entire sample.

2. Drug Release from Powders Containing Anesthetic Bases

The bupivacaine (base)-polylactide powders were a yellow color, due apparently to degradation of the drug. This degradation is also presumably the reason for the 30% assay value of most of these powders. The apparent in vitro drug release is shown in Figure 1 and demonstrates an excellent 12 hour continuous release profile. The effect of size on this drug release is minor and does not follow the logical order of smaller particles releasing drug more rapidly. Unsieved particles of pure drug dissolved considerably more rapidly.

The etidocaine (base) powders were white, and the assay values agree with the amount of drug initially added to the polymer solution. Again there is a close family of curves (Figure 2) with some discrepancies in the size to rate of release correlation. This in vitro release profile is considerably better than that for any previous homogeneous system developed on this program. However, a similar diffusion study using pure, unsieved, etidocaine (base) powder showed a similar slow release profile.

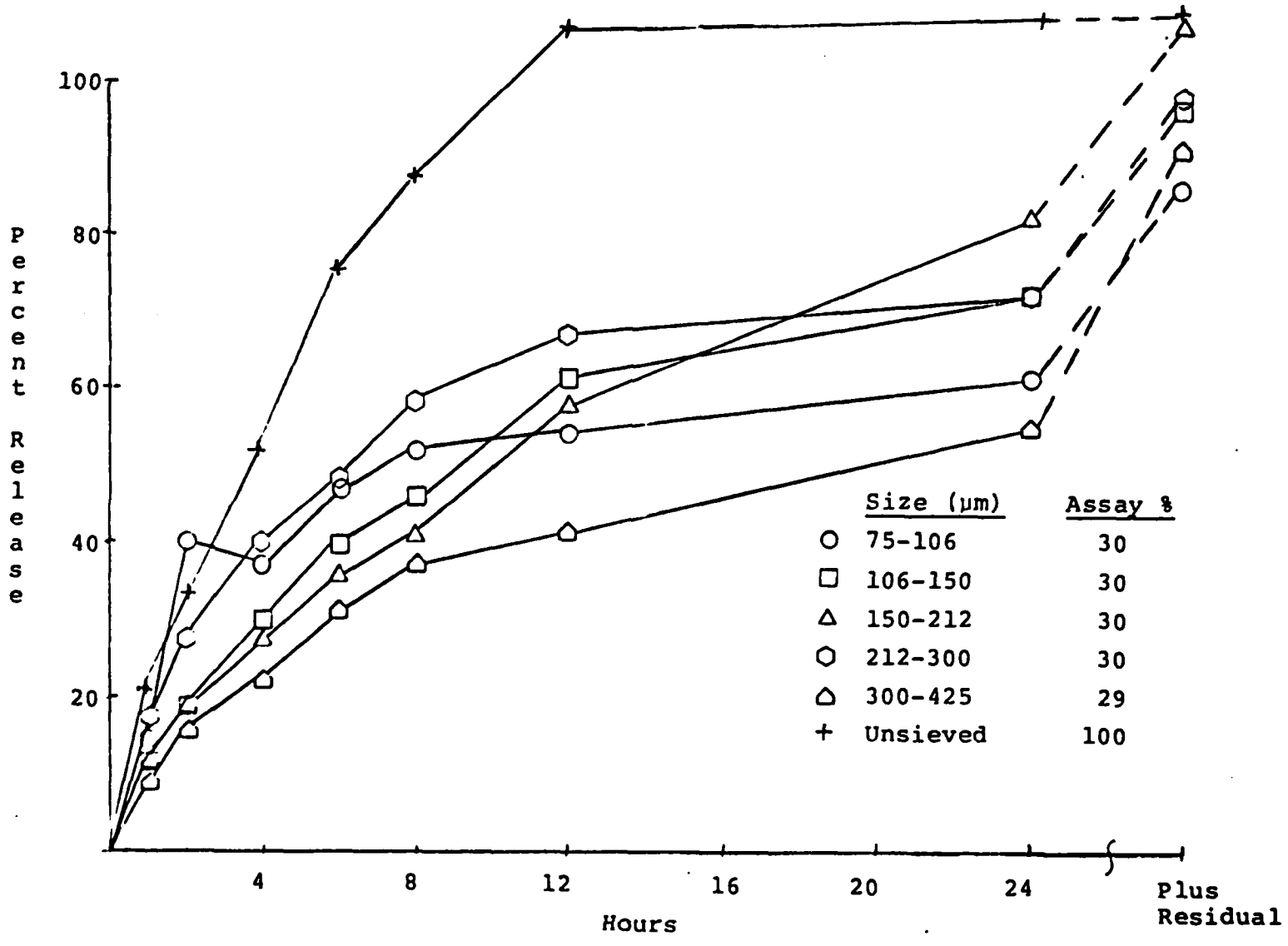


Figure 1 Bupivacaine (base) Release into Buffer of 20% Drug in Polymer Powder Samples and Pure Drug

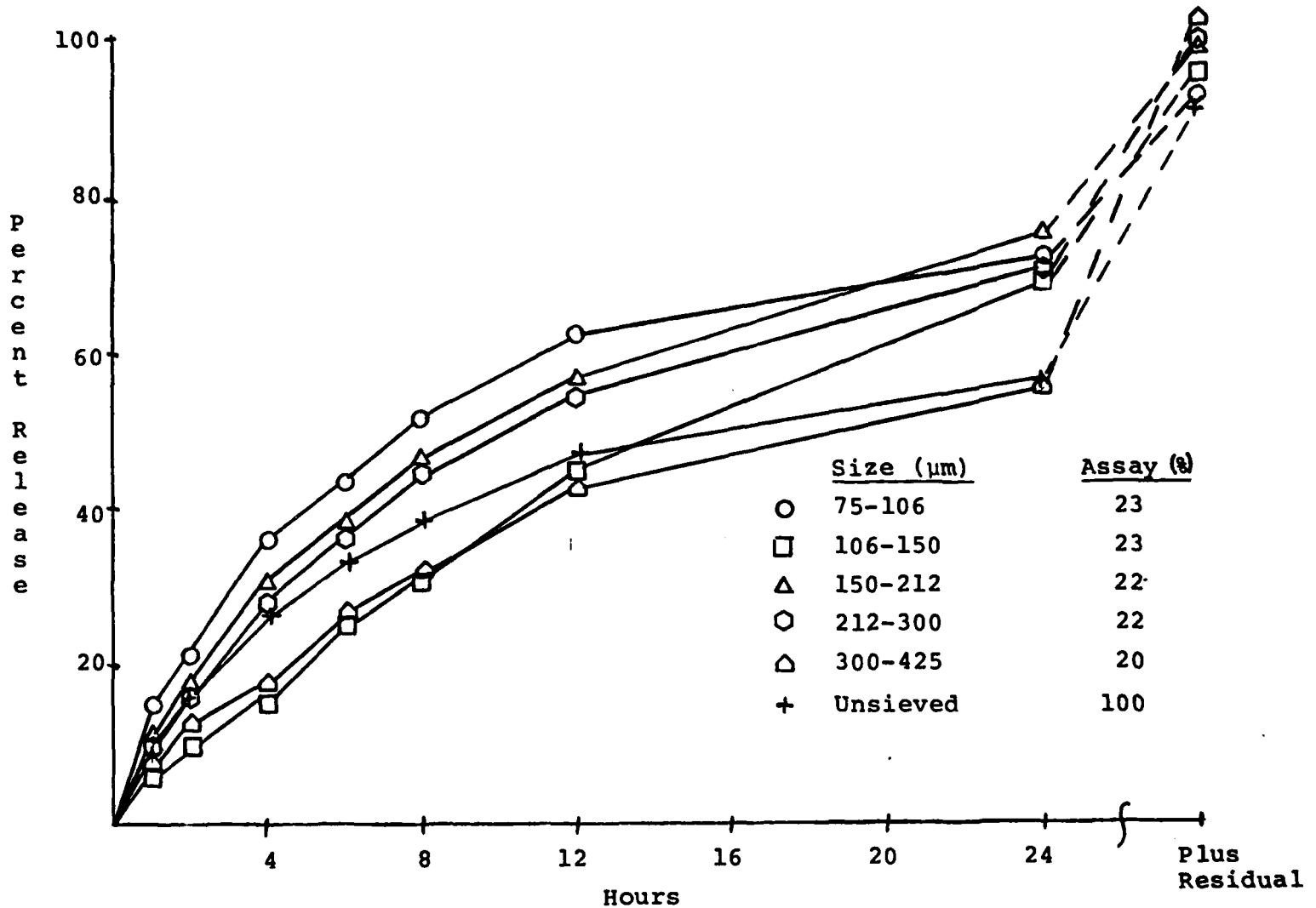


Figure 2 Etidocaine (base) Release into Buffer of 20% Drug in Polymer Powder Samples and Pure Drug

3. Drug Release from Fabrics Containing Anesthetic Bases

Solutions up to and including 7 percent bupivacaine (base) or 15 percent etidocaine (base) and 10 to 11 percent polymer were prepared in methylene chloride. These solutions sprayed thick, fibrous mats on the gauze. However, these 40% bupivacaine and 60% etidocaine fabrics released very little drug in in vitro tests (Figures 3 and 4). An 80 percent drug to polymer system containing 9 percent polymer in methylene chloride sprayed less fibrous material. The 100% drug solution of much lower viscosity did not spray well. This yielded a very fine non-fibrous deposit of drug on the gauze, but it was a very adherent layer. The 60% bupivacaine (base) fabrics (A and B) differed in their preparation only in the percent polymer in methylene chloride. The solution of higher viscosity (Solution B), containing 10% polymer, sprayed a more fibrous material which released drug more rapidly in vitro, than the less viscous Solution A containing 6 percent polymer. The 80 and 100 percent bupivacaine (base) fabrics released about 45 percent drug in six hours. In general, bupivacaine (base) fabrics released drug more quickly in a more continuous manner than etidocaine (base) fabric (Figures 3 and 4). This may be due to the greater solubility of bupivacaine (base) in buffer. Fabrics prepared with both bupivacaine and etidocaine (base) were white and have remained white now for several months.

4. PVP-I_2 Microcapsule Release

Povidone iodine release was studied in the standard equipment. However, a colorimetric measurement of iodine in the starch-iodide-buffer solution was used to determine the drug release. This approach was more rapid and sensitive than the previous thiosulfate titration procedure. The method gave good linearity with known quantities of povidone iodine. Selected samples of microcapsules were studied for drug release. The results were variable, with considerable active iodine being lost during the procedure. However, from data on the amount of active iodine released in one hour and the amount found in the microcapsules after one day, there was an indication of slow release of active iodine.

A study was designed to determine the cause of the active iodine loss. Conditions (temperature, iodide concentration, starch, aeration) were changed which might minimize the losses.

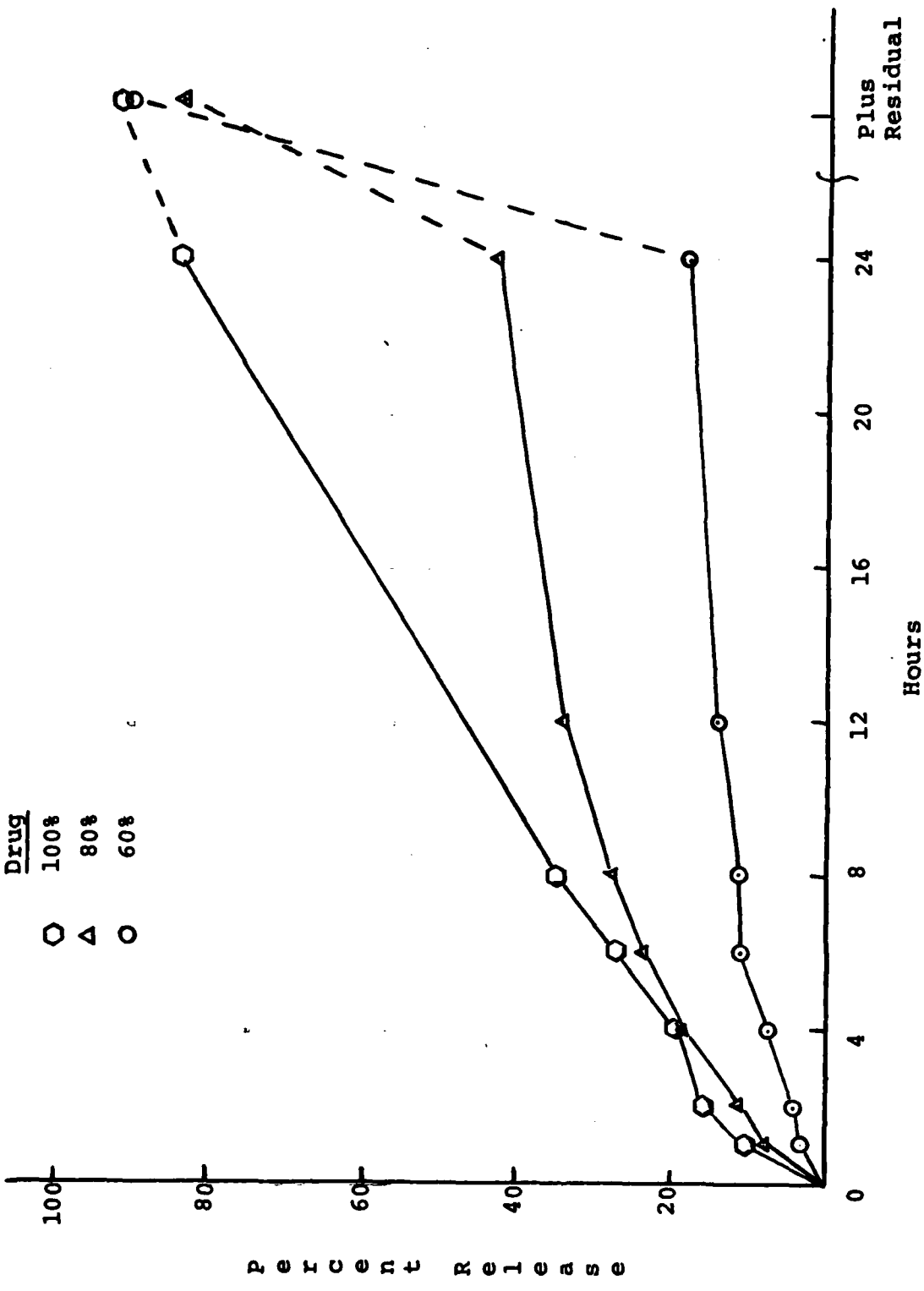


Figure 3 Etidocaine (base) Release from Non-Woven Fabric

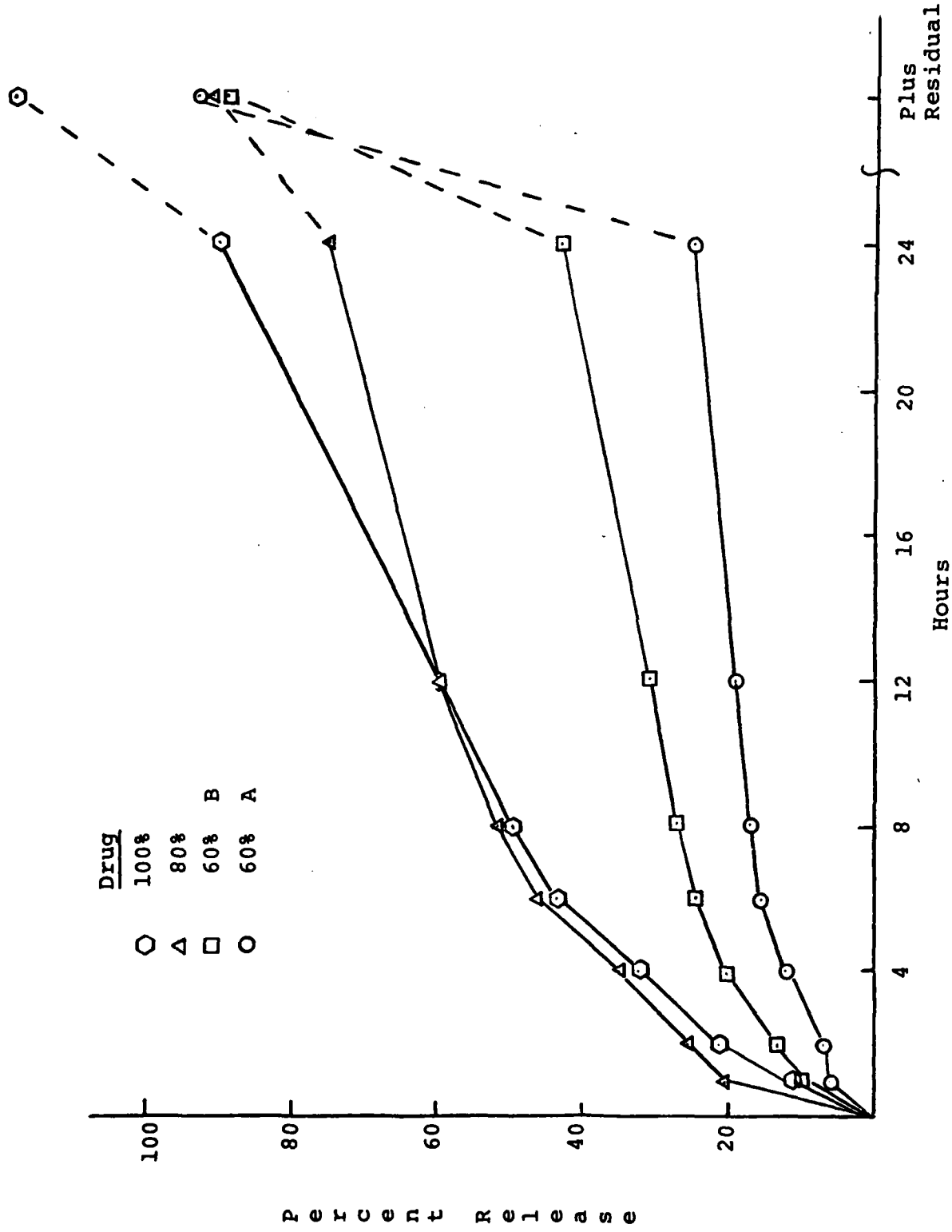


Figure 4 Bupivacaine (base) Release from Non-Woven Fiber Samples

The results of this experiment showed that temperature was the controlling variable, and by running the drug release experiment at room temperature (20°C) the loss of active iodine was minimal.

Iodine release was measured from the starting material and from microcapsules of 10, 20, and 30% polymer coating. The best results were with 30% coating, and these are shown in Figure 5. This data was the result of measurements in triplicate. The repeatability of the method is excellent as shown by the average of the standard deviations for the various time periods. The results were less precise for the smallest microcapsules. A sieve fraction of 212-600 microns would be 70% of the product (see Table 4). This material will be sent to Dr. Vincent for in vivo studies.

5. Benzalkonium Chloride Release from Non-Woven Fabric

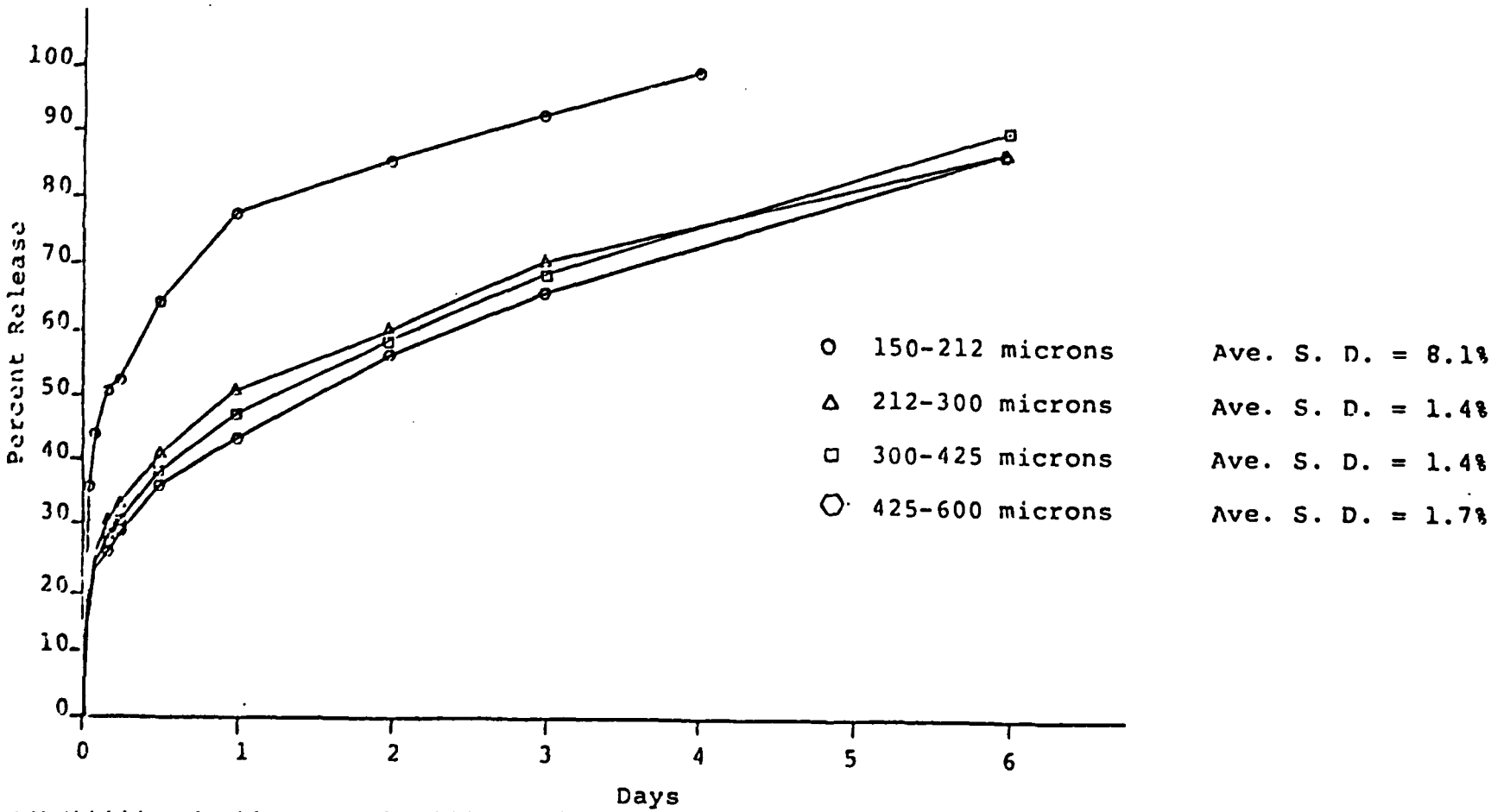
Fabrics were prepared with 5, 10, and 20% benzalkonium chloride (Maquat LC-12S). Practically no continued drug release was obtained with 5 and 10% loading of the drug (BAC), but about 15% of the drug was released immediately. Samples were then prepared at 20, 25, 30, and 40% drug; the resulting drug release is shown in Figure 6.

Our standard fabric uses 50 ml of solution and sprays a fabric of about 10 mg/cm^2. At 20% drug, we would have 2 mg of drug per cm^2. About 30% of this drug is released immediately, which is 600 µg/cm^2. Since this is at least 10 times too much, for use as an antiseptic, we considered methods to spray a mixture of fibers in order to prepare a wound dressing which will release drug in a manner similar to the 20% fabric.

6. Benzalkonium Chloride Release from Powders

Homogeneous powders were prepared with 20% Maquat LC-12S. Surprisingly the analysis of all the sieve fractions were 13.0± 1.0% based on the ultraviolet absorbance which is used for the assay and drug release method. There was no significant continuous drug release from the small powder samples. The drug release from the coarser powders is shown in Figure 7. Significant continued release is observed from particles of approximately 0.5 mm in diameter. In all cases (6) the residual BAC was 37.0 ± 3.9%. This was unavailable drug from either small or large particles.

Figure 5 Active Iodine Release From PVP-I_2 Microcapsules with 30% Polymer Coating (11-5-30)



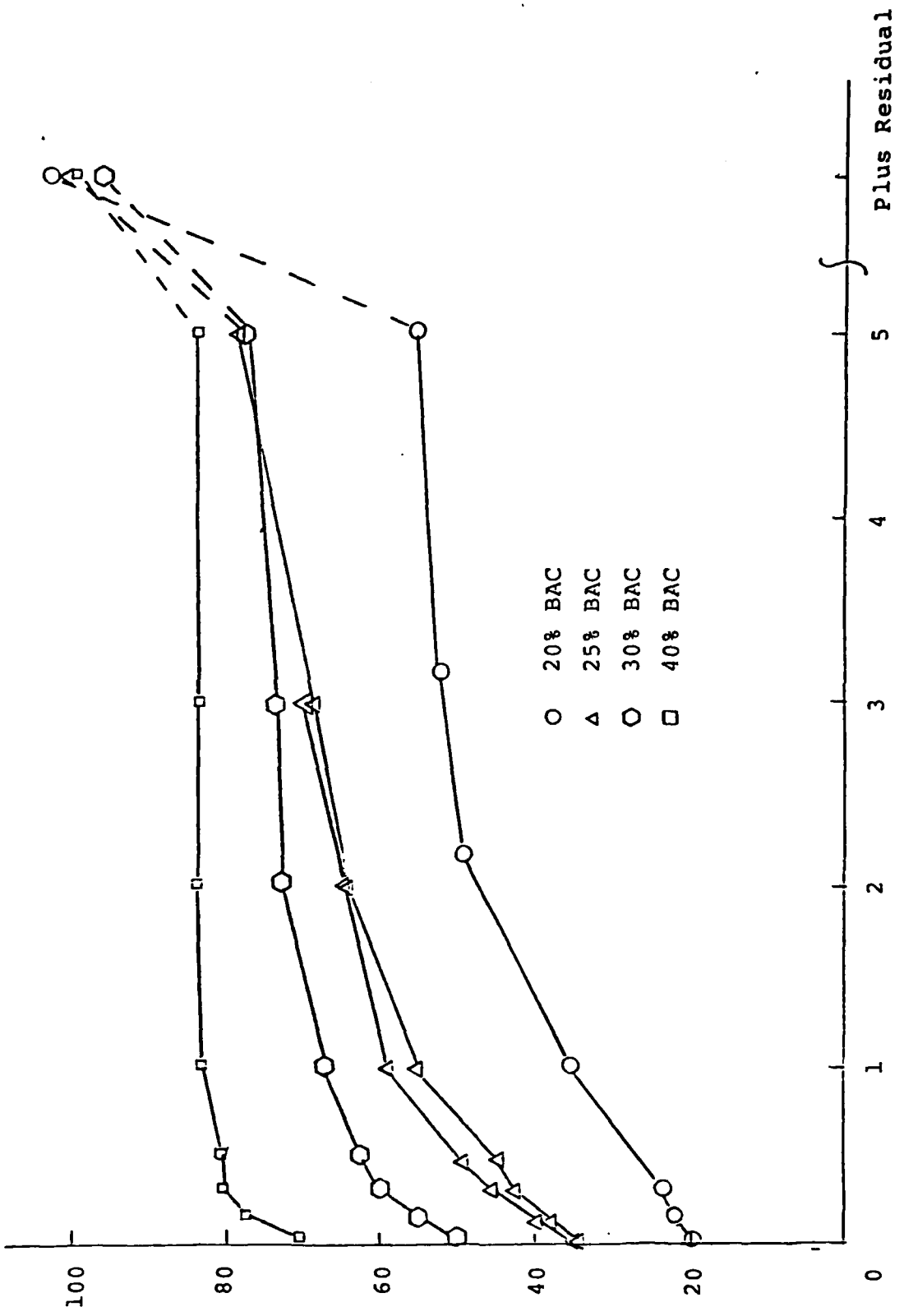
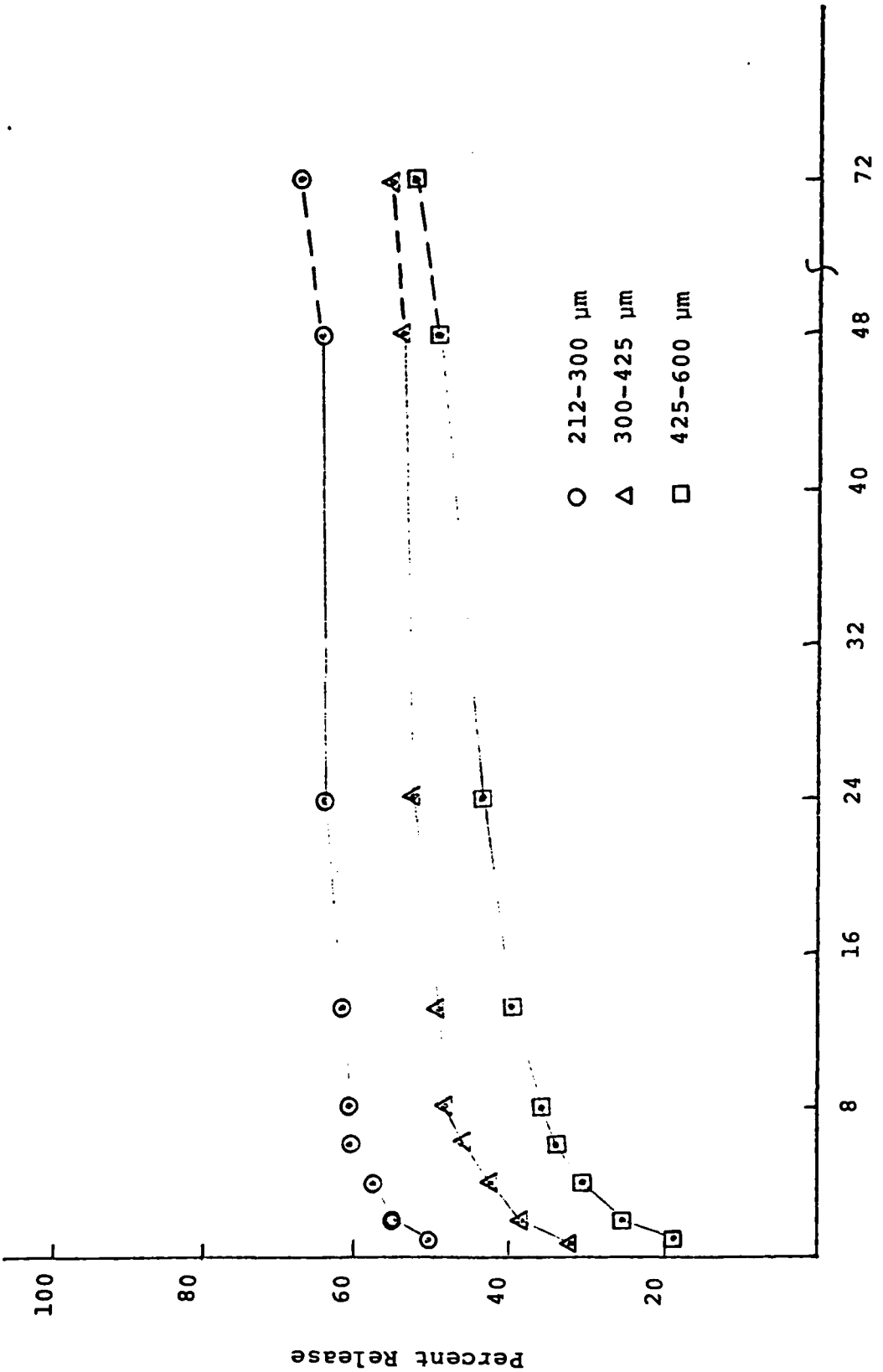


Figure 6 Release of Benzalkonium Chloride (BAC) from Polylactide Fabric

Figure 7 Release of Benzalkoniam Chloride from 13% Drug Powders of Various Sizes



C. Drug Release and Assay of Stored Samples

In the preceeding report, four powder samples, including the polymer-povidone-iodine powder prepared with the high molecular weight Napp material, were analyzed after one year of storage. During this period the stored povidone iodine BASF 17/12 powder was analyzed. Sustained release had not been achieved previously. However, approximately the same quantity of active iodine was released one year later, under all storage conditions (Table 7).

No fabric samples had been stored for one year at the time of the previous report. Four samples were analyzed during this period, as shown in Table 8. Some release of active iodine was observed in those PVP-I_2 fabric samples which were stored at room temperature and above. However, there was no significant loss of active iodine from any of these PVP-I_2 fabrics. The lidocaine (base) fabrics appear to release their drug more rapidly after storage at high temperature. The apparent loss of benzocaine from samples stored at 40°C agrees with results of previously tested benzocaine powder samples which had been stored at 40°C. The slower release of benzocaine from the samples stored at room temperature is surprising and may be a testing artifact. Etidocaine-HCl fabric samples show good stability after one year of storage.

D. Antiseptic Samples for Wound Evaluation

In discussing the antiseptic test protocol with Dr. Jack Vincent at USAIDR, a choice had to be made concerning the quantity of povidone-iodine to be used in the wound dressing. We had shown (Annual Summary Report, 23 June 1982, pp. 36-40) that 10 mg/ml of povidone iodine as pure drug or as 40% fabric was bacteriostatic in a tryptic soy broth which was inoculated with Bacillus subtilis. However, the equivalent volume of fluid in a test wound is not known. Faddis, Daniel and Boyer (1977) injected 100 mg of povidone iodine in a 2 ml volume, into the knee joint of 2 kg rabbits. This caused only minimal tissue damage. Much less material is normally used as an antiseptic dressing. A 3" x 9" Betadine^R Antiseptic Gauze Pad contains about 3.5 grams of Betadine Solution, or 350 mg of povidone iodine. This is about 2 mg of drug per cm^2 of dressing. We therefore decided to apply approximately 4 mg/cm^2 as slow release preparations.

TABLE 7

ASSAY AND DRUG RELEASE OF POWDERS AFTER ONE YEAR OF STORAGE

Sample	Hours of Release	Original Data	One Year Later					
			40°C Dark Open	40°C Dark Sealed	R.T. Light Open	R.T. Dark Open	4°C Dark Open	4°C Dark Sealed
PVP-I_2	1	72	93		76	80		
BASF 17/12	6	79	93		76	80		
20% drug	24	79	93		76	80		
300-425 μm	Assay %	(20)	15		16	17		

TABLE 8

ASSAY AND DRUG RELEASE OF FABRICS AFTER ONE YEAR OF STORAGE

Sample	Hours of Release	Original Data	One Year Later					
			40°C Dark Open	40°C Dark Sealed	R.T. Light Open	R.T. Dark Open	4°C Dark Open	4°C Dark Sealed
PVP-I_2	1	0	18		0	0		0
BASF 17/12	6	0	27		24	27		0
20% drug	24	0	27		24	27		0
	Assay %	(20)	17		17	16		15
Lidocaine (base)	1	36	91		74	75		41
20% drug	6	78	94		78	80		67
	24	96	95		82	80		72
	Assay %	(20)	23		25	22		34
Benzocaine	1	8	14		1	3		18
20% drug	6	25	24		6	10		30
	24	44	37		14	23		45
	Assay %	(20)	14		22	24		23
Etidocaine·HCl	1	28	24		30	28		
20% drug	6	52	40		46	43		
	24	65	55		60	60		
	Assay %	(20)	23		23	23		

Since our fabrics are about 10 mg/cm^2, the 40% povidone iodine fabric would contain 4 mg/cm^2, as normally prepared. Microcapsules that contain about 60% drug (30% polymer on 80% drug core) would be applied at about 7 mg/cm^2.

For benzalkonium chloride much smaller quantities are required for a bacteriostatic effect. Zephiran is sold as a 1/750 dilution (1,333 ppm). This concentration is required for Pseudomonas bacteriocidal activity. For diapers about 400 ppm is used, which corresponds to approximately 20 µg/cm^2 (personal communication, R. DeWolf, Mason Chemical Co., Chicago, IL). Edlich, et al (1969) tested both povidone iodine and benzalkonium chloride. They used a 0.1% solution of BAC for irrigation of contaminated wounds. Larger quantities can be expected to have toxic effects (Gosselin et al, 1976), including a curare-like paralysis of skeletal muscles. The USAIDR test protocol (Vincent, Setterstrom, Hollinger, 2 November 1982, "In Vivo Evaluation of a Wound Dressing Containing Poly-L(-)lactide and Povidone Iodine") includes both the effect on antiseptic efficacy and the effect on wound healing.

Based on this information we chose the following non-woven fabric materials for the initial in vivo studies (Table 9). Strips of non-woven fabric which were at least 1.5 cm wide and about 8 cm long were sent to Dr. Vincent. The backing is Parke-Davis Gauze bandage. The strips can be cut with surgical scissors to give the correct dimensions for each wound. In order to achieve continuous release of a small quantity of BAC, a 20% BAC/polymer solution was sprayed on top of a polymer fabric. In vitro studies indicate a continued release of similar samples. The samples were handled with surgical gloves and heat sealed in plastic envelopes prior to shipment.

Preliminary information was received by telephone from Dr. Vincent on February 22, 1983. Ten animals were used with each type of bandage for measurement of the antiseptic efficacy. The same technique had been used to evaluate a poroplastic membrane, generating reproducibly (100% morbidity) contaminated wounds Vincent (personal communication, 1982). However the BIOTEK fabric wound dressings were more absorbant and the control dressings provided contaminated wounds in only 3 of 10 cases (30%). In the test animals, 0% of the PVP-I_2 dressings produced contaminated wounds (0/9) and 10% of the BAC treated sites were contaminated (1/10). Dr. Vincent plans to modify the procedure to insure infection at the control sites when using polylactide control dressings.

TABLE 9

INITIAL SAMPLES SENT FOR IN VIVO EVALUATION ON WOUND HEALING OF ARTIFICIALLY CONTAMINATED WOUNDS

Sample	Thickness (mm)	Fabric Wt. mg/cm^2	Drug %	Drug Wt. mg/cm^2
Control	1.04±0.15	14.8	0	0
PVP-I_2	1.19±0.20	19.8	40	7.9
BAC	1.12±0.25	15.4	2.7	0.42

III. REFERENCES

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